of 35 U.S.C. § 112 for an alleged lack of enablement. Applicants respectfully argue against this rejection. The Examiner characterizes pending claim 1 as being directed to a method of activating CTLs in an animal having a tumor burden (pages 2-4 of the Office Action). In particular, the Examiner states at page 3 that this 112 rejection only applies to the claimed method of activating CTLs in "mice with a tumor expressing HER-2/Neu". The Examiner, based on this claim characterization, then states that the specification does not support CTL activation in tumor loaded animals.

Pending claim 1 is reproduced, *in haec verba*, below.

A method of activating cytotoxic T lymphocytes *in vivo*, wherein said cytotoxic T lymphocytes (CTLs) specifically target malignant cells that express a HER-2/Neu protein, the method comprising the step of immunizing an animal with the polypeptide of SEQ ID NO:10.
(Claim 1 as twice amended, Amendment of August 28, 2002)

Claim 1 does not contain the limitation "mice with a tumor expressing HER-2/Neu". Absent this limitation, the Examiner's rejection is not well founded and is without merit. Applicants respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 103

The Examiner has further rejected claim 1 under 35 U.S.C. § 103 as allegedly being obvious over Grey et al., taken with Cheever et al., Engleman et al., and Yoshino et al. This is a new rejection, not previously raised by the Examiner. The

Examiner characterizes Grey as teaching 1) the injection of putative CTL epitopes into transgenic mice to induce CTL activation, 2) the identification of immunogenic peptides including SEQ ID NO:10, and 3) that peptides having an A2 binding affinity of at least 0.010 are capable of inducing CTLs. The Examiner characterizes Cheever as teaching that p185 HER-2/Neu peptides, including SEQ ID NO:10, are suitable for stimulating $CD8^+$ T cells. The Examiner characterizes Engleman as teaching that Jurkat cells are human leukemia cells. The Examiner characterizes Yoshino as teaching tumor cell lines that express HER-2/Neu and methods for testing cell lysis. Based on these characterizations, the Examiner concludes that it would have been obvious to one of skill in the art to take the peptides taught by Grey or Cheever and test the ability of HER-2/Neu peptides to activate CTLs *in vivo*.

Applicants argue against this rejection for the reasons that follow. The Examiner relies on Grey as teaching that SEQ ID NO:10 binds to A2 with a relative affinity of 0.15 and the statement of Grey that all peptides with a relative binding to A2 of greater than 0.01 are capable of inducing CTL (page 76, lines 31-33). Applicants do not dispute the A2 binding data. Applicants respectfully submit that the alleged A2 binding/CTL association of Grey is inapposite to the HER-2/Neu peptides in general and SEQ ID NO:10 specifically. It can be seen from Table 24 of Grey (the only data relating A2 binding and CTL induction) that the only peptides tested were derived from HIV polymerase. Further, the data in Table 24 *per se* do not support the conclusion of Grey.

Peptide WILRGTSFV has a relative binding of 0.018 (80%

greater than 0.01) yet has no CTL activity. It is mere speculation that non-HIV peptides having a relative binding of greater than 0.01 will induce CTLs.

The deficiencies of Grey cannot be cured by Cheever. Cheever neither teaches nor even suggests *in vivo* CTL activation. The only mention in Cheever of CTL activation is Example 2, limited to *in vitro* activation.

Thus, even if one were to combine the teachings of Grey and Cheever, one of skill in the art would not expect to arrive at the presently claimed invention with any reasonable expectation of success. Rather, at best, Grey and Cheever can only be viewed as an invitation to experiment, a standard consistently viewed by the courts as being insufficient to sustain a 103 rejection.

In view of the above, Applicants respectfully request withdrawal of this rejection.

SUMMARY

For the reasons set forth above, Applicants respectfully submit that the claim is now in a condition of allowance. An early notification to that effect is hereby earnestly solicited.

Respectfully submitted,

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